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EXAMINER

ROBINSON, H

ART UNIT

PAPER NUMBER

1653

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
**09/437,912**

Applicant(s)  
**McCrae**

Examiner  
**Hope Robinson**

Art Unit  
**1653**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Apr 26, 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above, claim(s) 17, 18, 20, 21, and 23-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16, 19, and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4, 6, 8 20) ☐ Other:

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### **DETAILED ACTION**

1. Applicant's election with traverse of Group I (claims 1-16, 19 and 22) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the restriction is not proper if the search and examination of an entire application can be made without serious burden. Applicant argues that in the present case there is no serious burden in searching the claimed invention, regardless of whether the claim groups are independent or distinct. Applicant also argues that if the central feature of an invention is a composition containing certain compounds, USPTO practice is to direct a patentability search to the compound itself, even if the claims are directed to a method of using the compound or composition. Applicant also notes that both Groups II and III are in class 435. Applicant contends that because the compositions of Group I would encompass the methods of use in Groups II and III, there is no serious burden in searching and examining Groups I, II and III in the same application.

Applicant's arguments have been fully considered but are not persuasive. Group I encompasses the claimed composition and a method of using the composition. Groups II and III encompasses alternative ways of using the claimed composition. Applicant argues that "in the present case there is no serious burden in searching the claimed invention, regardless of whether the claim groups are independent or distinct". This citation from MPEP Chapter 800 section 802.02 is limited as the chapter goes on to say that there are two criterias for proper requirement for restriction. The inventions must be independent (there is no disclosed relationship between

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the two or more subjects disclosed, they are unconnected in design, operation, or effect) or distinct (two or more subjects are disclosed are related, for example combination and part (subcombination), process and apparatus for its practice, process and product made etc.) and are patentable (novel and unobvious) over each other. Therefore, the MPEP makes a clear distinction that if an invention is independent or distinct the requirement for restriction is proper. With regards to applicant's notation that Groups II and III are in the same class, note that the subclasses are different which indicates that the inventions have acquired a separate status in the art which exemplifies burden of search and that the search for Group I, II or III is not coextensive. Thus, the restriction requirement is proper, has been maintained and is final.

2. The drawings filed November 9, 1999 are acceptable.

### ***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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3. Claims 1-16, 19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the claim recites “and/or”, and it is unclear as to whether the slash refers to “and/or” or just “or”. The claim should be amended to recite “comprises an amino-terminal and carboxy-terminal protecting group” or “comprises an amino-terminal or carboxy-terminal protecting group”. Claim 1 is also indefinite because the claim recites that the pharmaceutical composition comprises a compound of the formula  $X_1$ -His-Lys-X-Lys- $X_2$  wherein X is any amino acid,  $X_1$  is from zero to twelve amino acids and  $X_2$  is from zero to twelve amino acids, and it is unclear as to the effect of 1-12 additional amino acids in the positions of  $X_1$  and  $X_2$  on the activity of the compound versus having zero amino acids in those positions. Furthermore, it is unclear what effect any amino acid at position X will have on the activity of the claimed compound especially since the specification on page 3 states that the peptides possess anti-angiogenic activity and that it is preferred that X is a nonpolar side chain.... most preferably X is Asn, Phe or His.

Claims 7 and 12 are indefinite as to the recitation of the phrase “substantial amino acid sequence homology”. It is noted that the specification on page 9 states that the phrase means an amino acid sequence homology greater than about 30%, preferably greater than about 60% etc. It is suggested that applicant rewrite the claim to read “a composition of claim 1 wherein the compound has greater than 30% sequence homology to the amino acid sequence....”, to make the

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claim definite as the limitations of the specification cannot be read into the claim and the term "substantial" is not specific the amount.

Claim 16 is indefinite because the claim appears to broaden the scope of claim 1 from which it depends, as the claim recites "administering to a mammal an effective amount of a composition according to claim 1" instead of "administering to a mammal an effective amount of the composition according to claim 1". It implies that the composition in claims 1 and 16 are different. Further, the method does not provide any steps on how to administer or how much to administer or how long to administer to result in inhibition of angiogenesis (see also claims 19 and 22).

Claims 2-15 are indefinite because the claims depend from a rejected based claim.

### ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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4. Claims 1-3, 5, 7-10 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Halazonetis et al. (U.S. Patent No. 6,245,886, December 4, 1997).

Halazonetis disclose pharmaceutical compositions of compounds and methods of using these compositions therapeutically. Halazonetis disclose the sequence contained in claim 1 where X can be any amino acid,  $X_1$  is zero-twelve amino acids and  $X_2$  is zero to twelve amino acids. Halazonetis disclose in SEQ ID NO: 21 the following sequence His-Lys-Ser-Lys-Lys which means that X is Ser (as in claim 3),  $X_1$  is zero amino acid and  $X_2$  is 1 amino acid. The sequence disclosed by Halazonetis also meets the limitation of claims 2 and 5 which requires  $X_1$  and  $X_2$  to be from zero to six amino acids or zero amino acids (as in item (i) of claims 5 and 10). In addition, Halazonetis disclose a sequence that has "substantial amino acid sequence homology to the amino acid sequence recited in claim 7 as the specification defines this as being "greater than about 30%" (see page 9). Note that the sequence recited in claim 7 is HGHEQQHGLGHG-**HKFK**-LDDLEHQGGHV where X is Phe,  $X_1$  is twelve amino acids and  $X_2$  is twelve amino acids and the portion of the sequence **HKFK** aligns with the sequence taught by Halazonetis **HKSK** providing substantial homology (see also claim 12 where the sequence **HKNK** is taught). As the claims have the limitation where X can be any amino acid; and  $X_1$  and  $X_2$  can be zero the limitations of the claims are met by this reference.

5. Claims 1-3, 5, 7-10 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Halazonetis et al. (WO 96/25434, August 22, 1996).

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Halazonetis disclose pharmaceutical compositions of compounds and methods of using these compositions therapeutically. Halazonetis disclose the sequence contained in claim 1 where X can be any amino acid,  $X_1$  is zero-twelve amino acids and  $X_2$  is zero to twelve amino acids. Halazonetis disclose in SEQ ID NO: 21 the following sequence His-Lys-Ser-Lys-Lys which means that X is Ser (as in claim 3),  $X_1$  is zero amino acid and  $X_2$  is 1 amino acid. The sequence disclosed by Halazonetis also meets the limitation of claims 2 and 5 which requires  $X_1$  and  $X_2$  to be from zero to six amino acids or zero amino acids (as in item (i) of claims 5 and 10). In addition, Halazonetis disclose a sequence that has "substantial amino acid sequence homology to the amino acid sequence recited in claim 7 as the specification defines this as being "greater than about 30%" (see page 9). Note that the sequence recited in claim 7 is HGHEQQHGLGHG-**HKFK**-LDDDLHQGGHV where X is Phe,  $X_1$  is twelve amino acids and  $X_2$  is twelve amino acids and the portion of the sequence **HKFK** aligns with the sequence taught by Halazonetis **HKSK** providing substantial homology (see also claim 12 where the sequence **HKNK** is taught). As the claims have the limitation where X can be any amino acid; and  $X_1$  and  $X_2$  can be zero the limitations of the claims are met by this reference.

6. Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferreira et al. (WO 97/05258, February 13, 1997).

Ferreira disclose peptides for use in diagnostic and therapeutic methods. Ferreira disclose the sequence contained in claim 1 where X can be any amino acid,  $X_1$  is zero-twelve amino acids



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and  $X_2$  is zero to twelve amino acids. Ferreira disclose in SEQ ID NO: 113 the following sequence Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val which means that X is Phe (as in claims 3, 4, 6 and 11),  $X_1$  is three amino acids and  $X_2$  is two amino acids. The sequence disclosed by Ferreira also meets the limitation of claims 2 and 5 which requires  $X_1$  and  $X_2$  to be from zero to six amino acids or zero amino acids (as in item (i) of claims 5 and 10). In addition, Ferreira disclose a sequence that has "substantial amino acid sequence homology to the amino acid sequence recited in claim 7 as the specification defines this as being "greater than about 30%" (see page 9). Note that the sequence recited in claim 7 is HGHEQQHGLGHG-**HKFK**-LDDDLHQGGHV where X is Phe,  $X_1$  is twelve amino acids and  $X_2$  is twelve amino acids and the portion of the sequence **HKFK** aligns with the sequence taught by Ferreira **HKFK** providing substantial homology (see also claim 12 where the sequence **HKNK** is taught) As the claims have the limitation where X can be any amino acid; and  $X_1$  and  $X_2$  can be zero the limitations of the claims are met by this reference.

### ***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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7. Claims 1-3, 5, 7-10, 12-16, 19 and 22 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Halazonetis et al. (U.S. Patent No. 6,245,886, December 4, 1997) in view of Wachtfogel (The Journal of Biological Chemistry, vol. 269, no. 30, pages 19307-19312, 1994).

The teachings of Halazonetis et al. is above as applied to claims 1-3, 5, 7-10 and 12-15. Halazonetis do not explicitly teach a method of inhibiting angiogenesis. Wachtfogel teach that high molecular weight kininogen (HK) binds specifically to neutrophils and also inhibits the binding of fibrinogen (which binds to leukocyte) to neutrophils. Watchtfogel also teach that HK inhibits the binding of thrombin to platelets and endothelial cells (see page 19307).

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Halazonetis disclose the claimed peptide sequence and a pharmaceutical composition that is used in cancer therapy via inducement of apoptosis or growth arrest of abnormal cells (see columns 4-5). Furthermore, the secondary reference Wachtfogel teach the inhibition of endothelial cells, thrombin binding to platelets and that HK is involved in binding of neutrophils and the binding of fibrinogen (which binds to leukocyte).

One would be motivated to combine the teachings of the above references because the specification on page 1 discloses that the migrating endothelial cells proliferate and the sprouts merge to form capillary loops thus forming new blood vessel, thus, absent evidence to the contrary, angiogenesis is inhibited by the method taught by Wachtfogel because the references demonstrates the inhibition of endothelial cells by HK. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

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***Art of Record***

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Colman et al. (Blood, vol. 92, No. 10, November 15, 1998). Colman demonstrates the inhibition of angiogenesis by peptides derived from kininogen. Colman also teach that the results suggest that polypeptides from domain 5 of HK may be potent inhibitors of angiogenesis which could have potential for inhibiting tumor cell metastasis and invasion, diabetic retinopathy (neovascularization) and the abnormal remodeling in atherosclerosis.

***Conclusion***

9. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, Ph.D., can be reached at (703)308-2932.

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Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS 

Patent Examiner



KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER